Office Action Summary	Application No.	Applicant(s)	
	10/519,455	RAOULT, DIDIER M	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/25/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Species a drawn to Bacteria in the reply filed on October 11, 2007 is acknowledged. However, the election of Species is withdrawn.

2. Claims 1-14 are under consideration in this office action.

Priority

3. Receipt is acknowledged of a certified copy of the FR 02/08324 application referred to in the oath or declaration or in an application data sheet. However, should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a translation of the foreign application should be submitted under 37 CFR 1.55 in reply to this action. Further, to obtain priority Applicant needs to submit an amendment to correct the first line of the specification. Applicant should have included in the amendment of the instant specification the following: This application is a 371 of PCT/FR03/02050 filed 02/07/03, which claims foreign priority to FR 02/08324 filed 3/07/02.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on May 25, 2005 was filed. The submission is in compliance with the provisions of 37 CFR 1.97.

Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. The claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical errors. Therefore appropriate clarification is required because the claim language is unclear.

6. Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) With respect to claims 1-14, it is unclear what exactly is characterized in that it is controlled that said sample to be tested contains a human serum. Therefore clarification is required to overcome the rejection.

b) Dependant claims 2-12 and 14 refer to “Serological diagnosis as in claim 1” or “Diagnosis kit as in claim 13”, however the suggested claim language is to use of the article “The.” Therefore the suggested claim language is “The serological diagnosis method” or “The method” or “The kit”.

c) Regarding claim 5, the phrase "preferably" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05.

d) Regarding claim 5, the phrase "in particular" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05.

e) Claims 8 and 10, recite alternative limitations which are improperly expressed. Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a Markush group recites members as being “selected from the group consisting of A, B and C”. Another acceptable form recites “selected from 1, 2, 3, or 4.” Applicant may correct this by amending the claim to recite the appropriate language.

f) Claim 11 is drawn to a second antigen corresponding to the infectious microbial agent being a bacterium responsible for endocarditis. However, it is unclear what criterion is being used to determine what the corresponding features are. Thus the metes and bounds of this phrase are unclear and appropriate clarification is required to overcome the rejection.

g) Claim 12 is rejected because acronyms and/or abbreviations like H.I.V and C.M.V. must be spelled out when used for the first time in a chain of claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-9 and 12-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Dorval et al., (US Patent 5,561,045).

Claim 1 is drawn to an *in vitro* serological diagnosis method in which, in a sample to be tested, the presence is detected of antibodies specific to an infectious microbial agent, characterized in that it is controlled that said sample to be tested contains a human serum by detecting whether human immunoglobulins react with an antigen containing Protein A from a *Staphylococcus aureus* bacterium. Claim 2 is drawn to a characterization in that : **-** the sample to be tested is caused to react with a first antigen (Ag_1) containing Protein A, preferably all or part of a *Staphylococcus aureus* bacterium containing Protein A, and - the presence is detected of an antigen-antibody reaction product (Ag_1- Ac_1) in which the antibody (Ac_1) is a human immunoglobulin, by causing said reaction product (Ag_1- Ac_1) to react with a detection substance which is a substance reacting with a human immunoglobulin and not reacting with said first antigen (Ag_1). Claim 3 is drawn to a characterization in that the following steps are performed, in which: a) on a solid-substrate-are-deposited said first antigen containing-protein

A (Ag_1), and at least one second antigen (Ag_2) which is characteristic of a microbial infectious agent (Ag_2), and b) the said first antigen (Ag_1) and second (Ag_2) antigen(s) are caused to react with a sample to be tested, and c) it is detected whether a human immunoglobulin (Ac_1) reacts with said first antigen (Ag_1) by causing the reaction product (Ag_1 -Ac_1) to react with a secondary detection antibody (Ac_2) which is a labeled anti-human immunoglobulin which does not react with protein A.

Claim 4 is drawn to the antigen being a whole *Staphylococcus aureus* bacterium containing protein A. Claim 5 is drawn to the presence is detected of a said reaction product (Ag_1- Ac_1) with an anti-human immunoglobulin (Ac_2) which is an immunoglobulin of animal origin, preferably goat or chick immunoglobulin. Claim 6 is drawn to the presence being detected of a reaction product of said first antigen (Ag_1) with a human immunoglobulin (Ac_1) using a substance labeled by fluorescent marking, in particular an anti-human immunoglobulin labeled with fluorescein. Claim 7 is drawn to the series of tests is performed at increasing dilutions of the sample to be tested and the detection substance (Ac_2) is applied which is an immunoglobulin conjugated with a fluorescent substance, and it is verified whether a reaction product (Ag_1- Ac_1- Ac_2) can be detected by fluorescence at a dilution of the sample to be tested of 1/200 or less. Claim 8 is drawn to the infectious microbial agent consisting of said second antigen being chosen from among micro-organisms containing a bacterium, a virus, a parasite or a fungus. Claim 9 is drawn to the second antigen (Ag_2) being an intracellular

bacterium or a virus. Claim 12 is drawn to the second antigen being a viral antigen chosen from among the H.I.V., C.M.V. or Epstein-Barr viruses.

Claim 13 is drawn to a diagnosis kit which can be used to implement the method of claim 1, characterized in that it includes at least one positive control controlling inclusion of a human serum in the sample to be tested comprising a said first antigen containing protein A (Ag_1) and reagents enabling the detection of the presence of a reaction product of said first antigen with a human immunoglobulin (Ac_1). Claim 14 is drawn to the kit including:- a solid substrate on which a said first protein A-containing antigen has been deposited (Ag_1) and a said second antigen corresponding to an infectious microbial agent (Ag_2) to be detected, and - a detection substance (Ac_1) to detect a reaction product of said first antigen with a human immunoglobulin containing a labeled anti-human immunoglobulin which is a goat or chick immunoglobulin labeled with fluorescent marking.

Dorval et al., teach processes that permit the ability to detect simultaneously a variety of classes of immunoglobulin specific for the same analyte (col.2, lines 30-34). Dorval et al., teach the enhancement of sensitivity using specific binding proteins like Protein A within immunoassays (col. 2, lines 35-40). Dorval et al., teach anti-IgA-IgG and anti-IgM-IgG and protein A (col. 3, lines 19-20). Dorval et al., teach a solid support with a first antigen containing Protein A, a second microbial antigen, the addition of the detection agent which is labeled anti-human immunoglobulin with does not react with Protein A, see

Figures 1a-1f. Dorval et al., teach a variety of kits with include the detection reagents, the binding protein A, and immunoglobulins (col. 4, lines 40-49). Dorval et al., teach labels to be chromophores, fluorophores, metal sols, enzyme labels and colorimetric particles (col. 6, lines 48-68). It is noted, that fluorescein is a common type of fluorophore. Dorval et al., teach the sensitivity of a wide variety of assays is enhanced with the use of the immunoglobulin and Protein A, including direct, indirect, competitive and sandwich type heterogeneous and homogenous assays (col. 9, lines 16-25). Dorval et al., teach the reagents may be advantageously in virtually any type of immunoassay where it is desirable to prevent the interaction of Protein A with a portion of an immunoglobulin; thus allowing the antigen to be bound to a solid phase and the presence of different classes of specific antibodies to be determined (col. 9, lines 25-33). Dorval et al., teach the detection of HIV virus (col. 9, lines 37-42).

Therefore Dorval et al., teach the instant invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dorval et al., (US Patent 5,561,045) in view of La Scola et al (Journal of Clinical Microbiology, 1996; 34(9): 2270-2274).

Claim 10 is drawn to the second antigen being Chosen from among bacteria of the genus *Rickettsia, Coxiella, Bartonella, Tropheryma, Ehrlichia, Chlamydia, Mycoplasma, Treponema, Borrelia,* and *Leptospira.* Claim 11 is drawn to the second antigen corresponding to the infectious microbial agent is a bacterium responsible for endocarditis.

Dorval et al., has been discussed above, however Dorval et al., do not teach the second antigen being *Bartonella* or a bacterium being responsible for endocarditis.

La Scola et al, teach serological cross-Reactions *between Bartonella Quintana, Bartonella henselae,* and *Coxiella burnetti. Bartonella Quintana,* is known to be associated with endocarditis, while *Bartonella henselae* is known to be associated diseases in AIDS patients (page 2270).La Scola et al., teach a method of performing serological diagnostic test for *Bartonella* and *C. burnetti* infections (page 2270). The prior art discloses immunoglobulin G (IgG) anti-phase I titer of equal to or greater than 1:800 and an IgA anti-phase II titer were considered diagnostic for infection. La Scola et al teach that human patients with titers of equal to or greater that 1:1,600 or antibody against *B. henselae* or *B. Quintana* antigens were also considered diagnostic for infection (page 2272). La Scola et al., teach positives being found (IgG, 1:100) (IgG 1:200) (page 2271).

The method of La Scola et al comprises the following steps: a) Serum samples were taken from patients; b) Bacterial antigen being deposited on 30 well microscope slides, and sera was serially diluted and applied to the wells; c) Slides were incubated in a moist chamber for 30 minutes, washed, dried and overlaid with labeled goat anti-human IgG antibodies; d) Interaction of antigen and antibody was observed (page 2271). La Scola et al., teach Western blotting was used to determine the interaction of antigen and antibody (page 2271).

Therefore, it would have been prima facie obvious at the time of applicants invention to modify the *in vitro* serological diagnosis method in which, in a sample to be tested, the presence is detected of antibodies specific to an infectious microbial agent, as taught by Dorval et al., wherein the modification incorporates the use of variety of microbial agents as taught by La Scola et al., in order to provide detection of a wide variety of agents. Furthermore, there is a reasonable expectation of success in incorporating the methods of Dorval et al., and La Scola et al., since both teach providing a sample to be tested is react with solid-substrate having a deposited first and second antigen and detecting whether the human immunoglobulin reacts with the first antigen, especially when the steps and components of the method have been combined with no change in their respective functions, thus the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to extend the methods taught by Dorval et al., and incorporate the

additional yet equivalent microbial antigens associated with AIDS and HIV into the *in vitro* serological diagnosis as taught by Dorval and La Scola et al., to arrive at the claimed invention with in order to allow enhancement of sensitivity using specific binding proteins like Protein A within immunoassays.

Conclusion

9. No claims allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached Monday thru Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Robert Mondesi, can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JaNa Hines/
Examiner, Art Unit 1645

/Mark Navarro/

Primary Examiner, Art Unit 1645